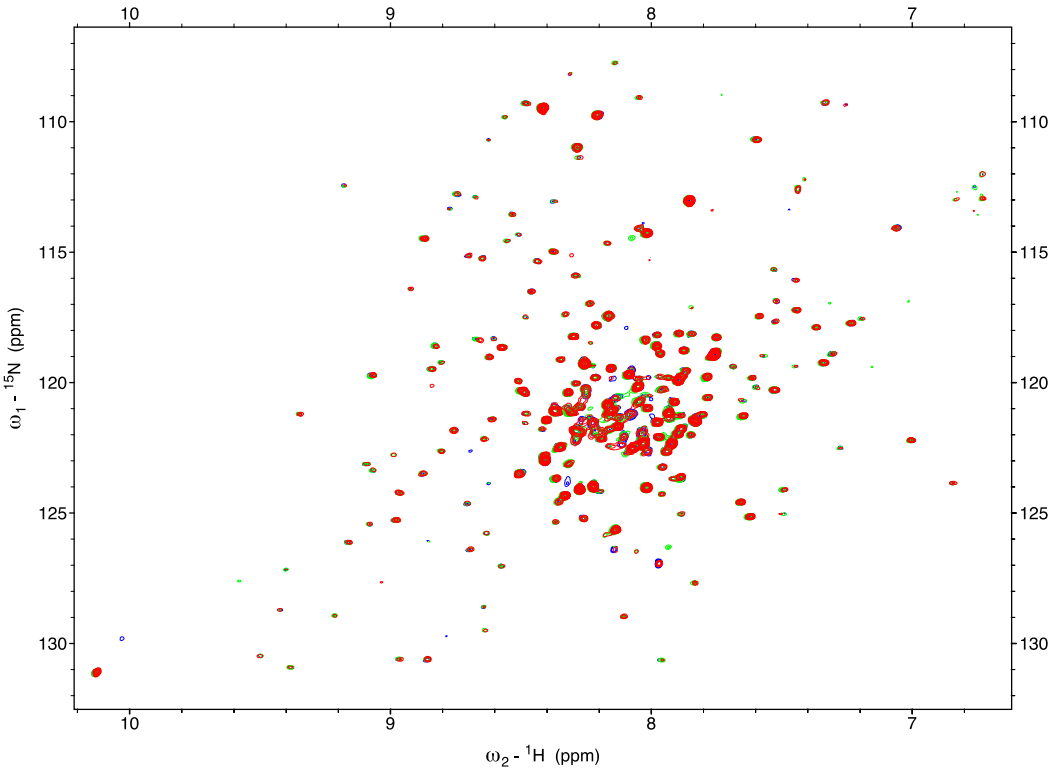

Figure S1.
Overlay of 900 MHz 2D ^{15}N-^{1}H TROSY-HSQC spectra [32,33] of 45 uM hsc-70 (395-604) without (blue), and with 160 uM (green) and 1600 uM DOPS (red) vesicles.

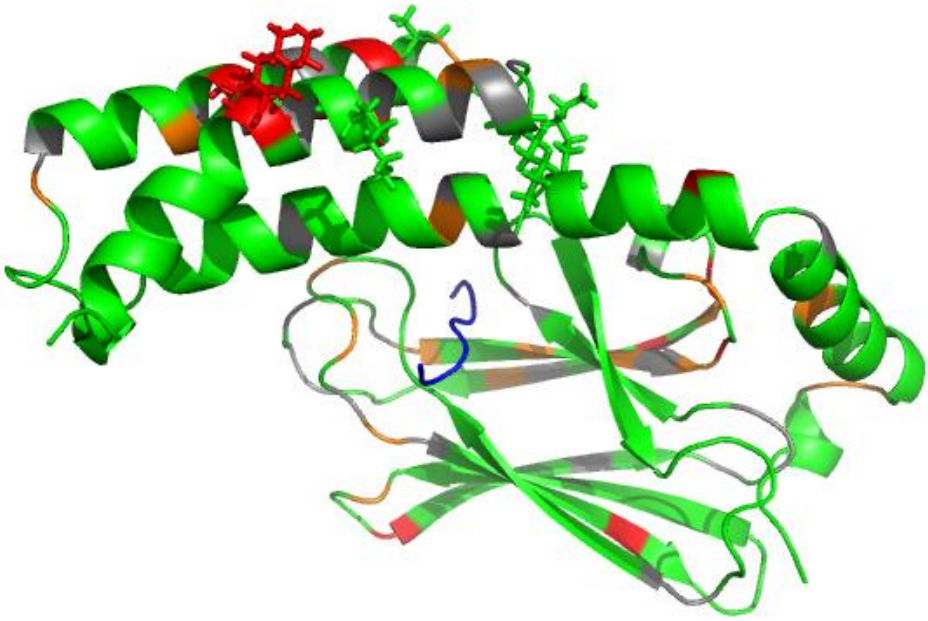

Figure S2.
Homology model of hsc-70 SBD based on the crystal structure of hsp-70 SBD complexed with NRLLLTG (4PO2.pdb).
The figure is color coded for the NH chemical shift perturbations resulting from adding 1.65 mM DOPS to 45 uM hsc-70 SBD in the presence of 165 uM of the hydrophobic TAU peptide KVQIINKKGCGMGHHHHHH blocking blocking the substrate binding cleft.
In green are NH shifts smaller than 2 standard deviations (SD); in orange 2 SD < CSP < 3 SD, in red CSP > 3 SD. In grey, unassigned / overlapped.
Residues R535, K573, K583, K589, K597 and K601 for which mutagenesis studies were carried out are rendered as sticks. The backbone of the bound NRLLLTG is shown in blue.

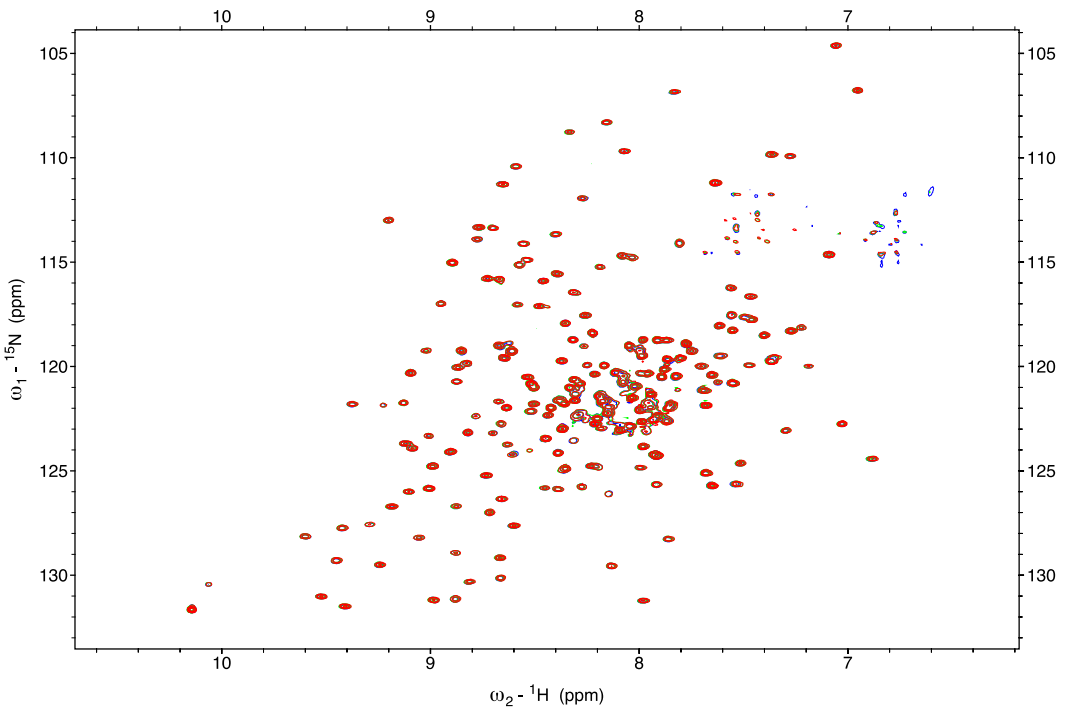

Figure S3.
Overlay of 600 MHz 2D ^{15}N-^{1}H TROSY-HSQC spectra hsc-70 (395-604) without (blue, hsc 80 uM), with sub-equivalent DOPS nano disks (green, hsc 57 uM , disks 36 uM) and supra equivalent DOPS nano disks (red, hsc 44 uM, Disks 55 uM).

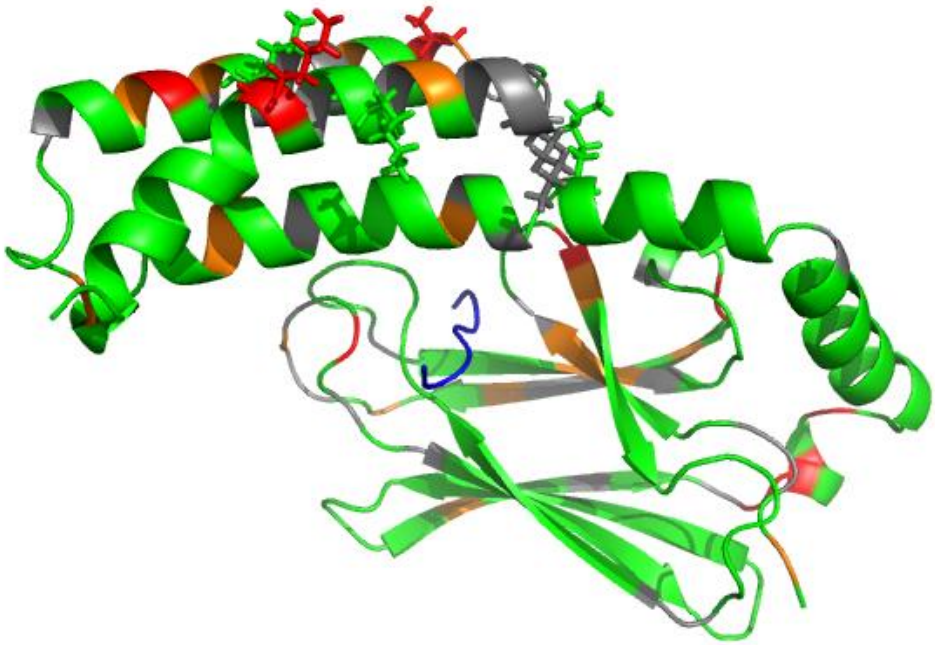

Figure S4.
Homology model of hsc-70 SBD based on the crystal structure of hsp-70 SBD complexed with NRLLLTG (4PO2.pdb).
The figure is color coded for the NH chemical shift perturbations resulting from adding 55 uM DOPS nanodisks to 44 uM Hsc70 SBD in the presence of 50 uM hydrophobic peptide MHHHHHHSSGVDLGTENLYFQ blocking the substrate binding cleft. Fig S2 is the corresponding histogram.
In green are NH shifts smaller than 2 standard deviations (SD); SD, in orange 2 SD < CSP < 3 SD, in red CSP > 3 SD. In grey, unassigned / overlapped.
Residues R535, K573, K583, K589, K597 and K601 for which mutagenesis studies were carried out are rendered as sticks. The backbone of the bound NRLLLTG is shown in blue.

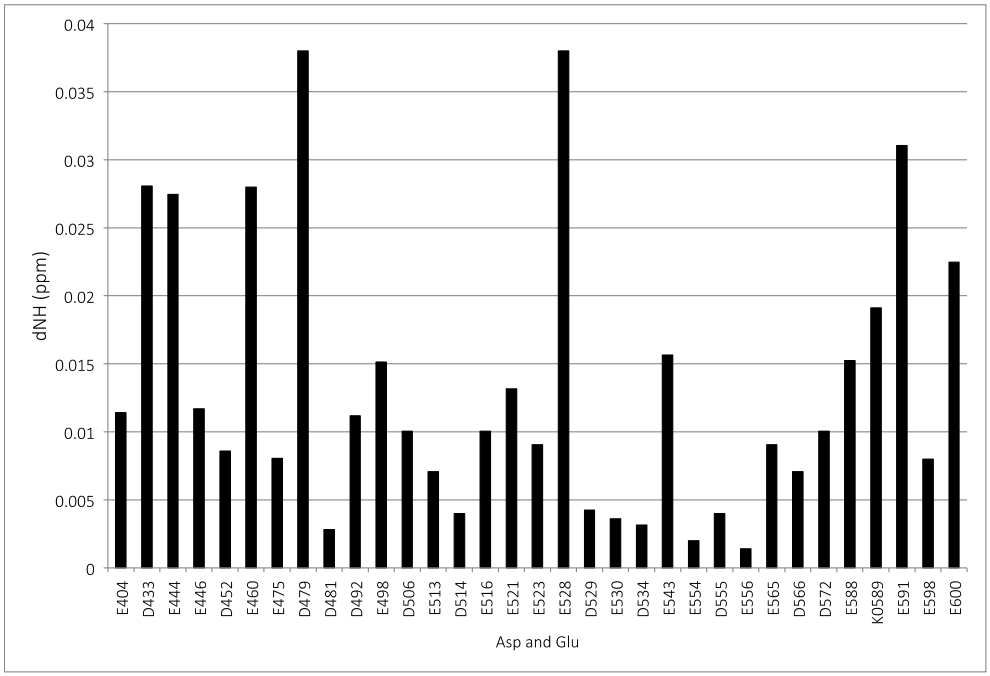

Figure S5.
Glutamate and Aspartate residue amide group chemical shift perturbations resulting from adding 1.65 mM DOPS to 45 uM hsc-70 SBD in the presence of 165 uM of the hydrophobic TAU peptide KVQIINKKGCGMGHHHHHH blocking the substrate binding cleft.

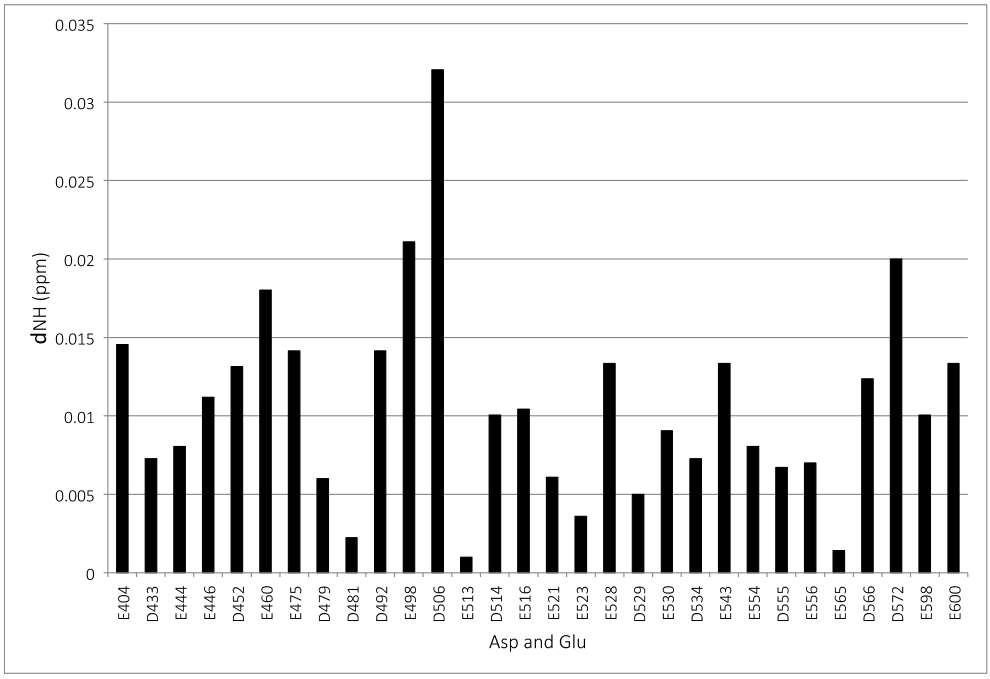

Figure S6.
Glutamate and Aspartate amide group chemical shift perturbations resulting from adding 55 uM DOPS nanodisks to 44 uM hsc-70 SBD in the presence of 50 uM hydrophobic peptide MHHHHHHSSGVDLGTENLYFQ blocking the substrate binding cleft.